

What is claimed is:

1. A method of treating or ameliorating an inflammatory disorder or an autoimmune disorder or one or more symptoms thereof, said method comprising  
5 administering to a subject in need thereof a prophylactically or therapeutically effective amount of one or more integrin  $\alpha_v\beta_3$  antagonists and a prophylactically or therapeutically effective amount of one or more immunomodulatory agents.
2. The method of claim 1 wherein said  $\alpha_v\beta_3$  antagonist is VITAXIN™ or an  
10 antigen-binding fragment thereof.
3. A method of treating or ameliorating an inflammatory disorder or an autoimmune disorder or one or more symptoms thereof, said method comprising  
15 administering to a subject in need thereof a prophylactically or therapeutically effective amount of one or more integrin  $\alpha_v\beta_3$  antagonists and a prophylactically or therapeutically effective amount of one or more anti-inflammatory agents.
4. The method of claim 3 wherein said  $\alpha_v\beta_3$  antagonist is VITAXIN™ or an  
20 antigen-binding fragment thereof.
5. A method of treating or ameliorating an inflammatory disorder or an autoimmune disorder or one or more symptoms thereof, said method comprising  
25 administering to a subject in need thereof a prophylactically or therapeutically effective amount of one or more integrin  $\alpha_v\beta_3$  antagonists and a prophylactically or therapeutically effective amount of one or more TNF- $\alpha$  antagonists.
6. The method of claim 5 wherein said  $\alpha_v\beta_3$  antagonist is VITAXIN™ or an  
30 antigen-binding fragment thereof.
7. A method of treating or ameliorating an inflammatory disorder or an autoimmune disorder or one or more symptoms thereof, said method comprising  
35 administering to a subject in need thereof a prophylactically or therapeutically effective amount of one or more integrin  $\alpha_v\beta_3$  antagonists and a prophylactically or therapeutically effective amount of one or more CD2 binding molecules.

8. The method of claim 7 wherein said  $\alpha_v\beta_3$  antagonist is VITAXIN™ or an antigen-binding fragment thereof.

5 9. The method of claim 1 or 2, wherein at least one immunomodulatory agent is a small organic molecule.

10. The method of claim 1 or 2, wherein at least one immunomodulatory agent is a T cell receptor modulator or a cytokine receptor modulator.

10 11. The method of claim 9, wherein the small organic molecule is methotrexate, leflunomide, cyclophosphamide, cyclosporine A, FK506, mycophenolate mofetil, rapamycin, mizoribine, deoxyspergualin, brequinar, a malononitriloamide, a steroid or a corticosteroid.

15 12. The method of claim 10, wherein the T cell receptor modulator is an antibody, peptide or a fusion protein which immunospecifically binds to a T cell receptor.

20 13. The method of claim 12, wherein the antibody that immunospecifically binds to a T cell receptor is a monoclonal antibody or an antigen-binding fragment thereof.

14. The method of claim 13, wherein the monoclonal antibody is a human or humanized monoclonal antibody.

25 15. The method of claim 13, wherein the monoclonal antibody is an anti-CD2 monoclonal antibody, an anti-CD4 monoclonal antibody, an anti-CD8 monoclonal antibody or an anti-CD40 monoclonal antibody.

16. The method of claim 12, wherein the fusion protein is CTLA4-Ig.

30 17. The method of claim 10, wherein the cytokine receptor modulator is a cytokine, a fragment of a cytokine, a fusion protein or an antibody that immunospecifically binds to a cytokine receptor.

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18. The method of claim 10, wherein the cytokine receptor modulator is a peptide, polypeptide, fusion protein or an antibody that immunospecifically binds to a cytokine.

19. The method of claim 17, wherein the antibody that immunospecifically binds  
5 to a cytokine receptor is a monoclonal antibody or an antigen-binding fragment thereof.

20. The method of claim 19, wherein the monoclonal antibody is a human or humanized monoclonal antibody.

10 21. The method of claim 17, wherein the antibody is an anti-IL-2 receptor antibody and anti-IL-12 receptor antibodies.

22. The method of claim 18, wherein the antibody that immunospecifically binds  
15 to a cytokine is a monoclonal antibody or an antigen-binding fragment thereof.

23. The method of claim 22, wherein the monoclonal antibody is a human or humanized monoclonal antibody.

20 24. The method of claim 18, wherein the antibody is anti-TNF- $\alpha$  antibody, an anti-IL-1 $\beta$  antibody, or an anti-IL-6 antibody.

25. The method of claim 17, wherein the cytokine is IL-4 or IL-10.

25 26. The method of claim 18, wherein the polypeptide is a fragment of a cytokine receptor that immunospecifically binds to a cytokine.

27. The method of claim 26, wherein the fragment is a portion of the extracellular domain of a TNF- $\alpha$  receptor.

30 28. The method of claim 3 or 4, wherein at least one anti-inflammatory agent is a non-steroidal anti-inflammatory drug.

29. The method of claim 27, wherein the non-steroidal anti-inflammatory drug is  
35 aspirin, ibuprofen, diclofenac, nabumetone, naproxen, or ketoprofen.

30. The method of claim 5 or 6, wherein the TNF- $\alpha$  antagonist is ENBREL™ or REMICADE™.

31. The method of claim 5 or 6 further comprising administering to said subject  
5 a prophylactically or therapeutically effective amount of methotrexate.

32. The method of claim 7 or 8, wherein the CD2 binding molecule is a peptide,  
polypeptide, fusion protein or an antibody that immunospecifically binds to a CD2  
polypeptide.  
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33. The method of claim 32, wherein the fusion protein is LFA-3TIP.

34. The method of claim 7 or 8 further comprising administering to said subject  
15 a prophylactically or therapeutically effective amount of a non-steriodal anti-inflammatory  
drug.

35. The method of claim 34, wherein the non-steriodal anti-inflammatory drug is  
aspirin, ibuprofen, diclofenac, nabumetone, naproxen, or ketoprofen.  
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36. The method of claim 7 or 8 further comprising administering to said subject  
a prophylactically or therapeutically effective amount of one or more immunomodulatory  
agents other than a CD2 binding molecule.

37. A method of treating or ameliorating an inflammatory disorder or an  
25 autoimmune disorder or one or more symptoms thereof, said method comprising  
administering to a subject in need thereof a prophylactically or therapeutically effective  
amount of one or more integrin  $\alpha_v\beta_3$  antagonists and a prophylactically or therapeutically  
effective amount of MEDI-507 or an antigen-binding fragment thereof.

38. A method of treating or ameliorating an inflammatory disorder or an  
30 autoimmune disorder or one or more symptoms thereof, said method comprising  
administering to a subject in need thereof a prophylactically or therapeutically effective  
amount of VITAXIN™ or an antigen-binding fragment thereof and a prophylactically or  
35 therapeutically effective amount of MEDI-507 or an antigen-binding fragment thereof.

39. The method of claim 37 or 38 further comprising administering to said subject a prophylactically or therapeutically effective amount of one or more TNF- $\alpha$  antagonists.

5 40. The method of claim 37 or 38 further comprising administering to said subject a prophylactically or therapeutically effective amount of methotrexate.

41. The method of claim 37 or 38 further comprising administering to said subject a prophylactically or therapeutically effective amount of one or more TNF- $\alpha$  antagonists and a prophylactically or therapeutically effective amount of methotrexate.

42. The method of claim 39, wherein at least one TNF- $\alpha$  antagonist is ENBREL™ or REMICADE™.

15 43. The method of claim 1, 3, 5, 7 or 37, wherein at least one integrin  $\alpha_v\beta_3$  antagonist is an anti-integrin  $\alpha_v\beta_3$  antibody.

44. The method of claim 44, wherein the anti- $\alpha_v\beta_3$  antibody is a monoclonal antibody or an antigen-binding fragment thereof.

45. The method of claim 45, wherein the monoclonal antibody is a human or humanized monoclonal antibody.

25 46. The method of claim 1, 2, 3, 4, 5, 6, 7, 8, 37 or 38, wherein the inflammatory disorder is asthma, encephalitis, inflammatory bowel disease, chronic obstructive pulmonary disease (COPD), arthritis, or an allergic disorder.

47. The method of claim 1, 2, 3, 4, 7, 8, 37 or 38, wherein the autoimmune disorder is rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Reiter's Syndrome, inflammatory bowel disease associated arthritis, an undifferentiated spondyloarthropathy, psoriasis, or an undifferentiated arthropathy.

48. The method of claim 1, 2, 3, 4, 5, 6, 7, 8, 37 or 38, wherein the subject is a human.

49. The method of claim 5, 6, 7, 8, 37 or 38, wherein the subject is a human who is or has previously been treated with one or more TNF- $\alpha$  antagonists.

50. The method of claim 5, 6, 7, 8, 37 or 38, wherein the subject is a human who is not currently being treated with a TNF- $\alpha$  antagonist or methotrexate.

51. The method of claim 5, 6, 7, 8, 37 or 38, wherein the subject is a human with an inflammatory disorder that is refractory to treatment with a TNF- $\alpha$  antagonist, a non-steroidal anti-inflammatory agent or methotrexate alone.

52. The method of claim 2, 4, 6, 8 or 38, wherein VITAXIN<sup>TM</sup> or an antigen-binding fragment thereof is administered orally, topically, intravenously, intramuscularly or subcutaneously to said subject.

53. The method of claim 37 or 38, wherein MEDI-507 or an antigen-binding fragment thereof is administered orally, topically, intravenously, intramuscularly or subcutaneously to said subject.

54. The method of claim 1, 3, 5, 7 or 37, wherein said integrin  $\alpha_v\beta_3$  antagonists are not small organic molecules.

55. The method of claim 1, 3, 5, 7 or 37, wherein at least one integrin  $\alpha_v\beta_3$  antagonist is a small organic molecule.

56. The method of claim 7 or 8, wherein said CD2 binding molecules are not small organic molecules.

57. The method of claim 7 or 8, wherein at least one CD2 binding molecule is a small organic molecule.

58. A method of treating or ameliorating an inflammatory disorder or an autoimmune disorder or one or more symptoms thereof, said method comprising administering to a subject in need thereof a prophylactically or therapeutically effective amount of VITAXIN<sup>TM</sup> or an antigen-binding fragment thereof, a prophylactically or

therapeutically effective amount of REMICADE™ or ENBREL™, and a prophylactically or therapeutically effective amount of methotrexate.

5 59. The method of claim 58, wherein the amount of VITAXIN™ or an antigen-binding fragment thereof administered to said subject is a dosage of about 0.1 mg/kg to 10mg/kg.

10 60. The method of claim 58, wherein the amount of REMICADE™ administered to said subject is a dosage of about 0.1 mg/kg to 10 mg/kg.

61. The method of claim 58, wherein the amount of ENBREL™ administered to said subject is a dosage of about 0.01 mg/kg to 10 mg/kg.

15 62. The method of claim 58, wherein the methotrexate administered to said subject is a dosage of about 0.01 mg/kg to 3 mg/kg.

20 63. A pharmaceutical composition comprising an integrin  $\alpha_v\beta_3$  antagonist, a TNF- $\alpha$  antagonist, and a pharmaceutically acceptable carrier.

64. A pharmaceutical composition comprising an integrin  $\alpha_v\beta_3$  antagonist, a CD2 binding molecule, and a pharmaceutically acceptable carrier.

25 65. The composition of claim 63 further comprising methotrexate.

66. The composition of claim 63 or 65, wherein the integrin  $\alpha_v\beta_3$  antagonist is VITAXIN™ or an antigen-binding fragment thereof.

30 67. The composition of claim 63, wherein the TNF- $\alpha$  antagonist is REMICADE™ or ENBREL™.

68. The composition of claim 64, wherein the CD2 binding molecule is LFA3TIP, MEDI-507, or antigen-binding fragment of MEDI-507.

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69. A pharmaceutical composition comprising VITAXIN™ or an antigen-binding fragment thereof, MEDI-507 or an antigen-binding fragment thereof, and a pharmaceutically acceptable carrier.

5 70. An article of manufacture comprising packaging material and a pharmaceutical composition in suitable form for administration to a human contained within said packaging material, wherein said pharmaceutical composition comprises VITAXIN™ or an antigen-binding fragment thereof, MEDI-507 or an antigen-binding fragment thereof, a pharmaceutically acceptable carrier, and instructions contained with said packaging  
10 material which suggests a dosing regimen for the prevention or treatment of an inflammatory disorder or an autoimmune disorder.

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